# A Review on Pharmacological Activities of

# *Bruguiera gymnorhiza*

by

Anika Mehnaz Dristy

ID: 17146049

A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons.)

Department Of pharmacy

Brac University

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## Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing my degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material that has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

**Student's Full Name & Signature:**

Anika Mehnaz Dristy

23.01.2022

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**Anika Mehnaz Dristy**

17146049

## Approval

The thesis titled "A Review on Pharmacological Activities of *Bruguiera gymnorhiza*" submitted by Anika Mehnaz Dristy (17146049) of Spring 2017 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 23rd January,2022.

**Examining Committee:**

Supervisor:
(Member)

23.01.2022

_______________________________

Dr. Farhana Alam Ripa
Assistant Professor, Department of Pharmacy
Brac University

Program Coordinator:
(Member)

_______________________________

Namara Mariam Chowdhury
Lecturer, Department of Pharmacy
Brac University

Departmental Head:
(Chairperson)

_______________________________

Dr. Eva Rahman Kabir
Professor, Department of Pharmacy
Brac University

# Ethics Statement

This study does not involve any kind of animal or human trial.

## Abstract

Medicinal plants are  great source of biologically active phytochemicals with therapeutic characteristics that have been recognized over time.In traditional medicine, many components of mangrove plants are used for their curative and defensive properties. This study aimed to review pharmacological properties of *Bruguiera gymnorhiza* and also its related phytochemicals. It is a significant medicinal plant, grows in mangrove areas, has so many economical values. In various research preparations, its extractions have shown a great impact on phytochemical and pharmacological activities. The most valuable phytochemicals are flavonoids, tannins, saponins, terpenoids, phenolic compounds, phytosterols, and terpenoids obtained from the plant's parts are discussed in this article.These bioactive phytoconstituents formed in plant tissues are mainly responsible for plants' different pharmacological effects.It has shown highly antidiarrheal, analgesic, antimicrobial, hepatoprotective, antihyperglycemic, antihyperlipidemic, antioxidant, etc activities due to these compounds that are explained in this paper and could be useful in the development of future pharmaceutical products.



**Keywords:** *Bruguiera gymnorhiza*; Medicinal Plant; Mangrove; Phytochemicals; Pharmacological;  Antioxidant

## Dedication

*Dedicated to my parents and my respectable supervisor of this project, Dr.Farhana Alam Ripa ma'am(Assistant Professor, Department of Pharmacy, Brac University)for their enormous support till the end.*

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A project is never the work of an individual. It is more than a combination of ideas, suggestions, review, contribution, and work involving folks. It cannot be completed without guidelines.

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# List of Acronyms

| | |
|---|---|
| CH | Catechin |
| QU | Quercetin |
| EA | Ellagic Acid |
| VL | Vanillin |
| GalN | Galactosamine |
| GSH | Glutathione |
| STZ | Streptozotocin |
| LPS | Lipopolysaccharide |
| LC | Liquid Chromatography |
| NMR | Nuclear Magnetic Resonance |
| GAP | Guaranteed Asset Protection. |
| HPLC | High-Performance Liquid Chromatography |
| CaMP | Cyclic Adenosine Monophosphate |
| PGE2 | Prostaglandin E2 |
| AST | Aspartate Aminotransferase |
| Alt | Alanine Aminotransferase |
| UDP | Uridine Diphosphate Galactose |
| LDL | Low-Density Lipoprotein |
| PUFA | Polyunsaturated Fatty Acids |
| ROS | Reactive Oxygen Species |

# Chapter 1-Introduction

## 1.1. Medicinal Plants

"**MEDICINAL PLANT"** which has chemicals, can be utilized for therapeutic reasons or as precursors regarding the manufacture of valuable pharmaceutical products. (Sofowora et al., 2013) These types of various plants use in ethnomedicine, some of which have medicinal properties which have great sources of components for the discovery and synthesis of medicines. (Rasool Hassan, 2012) Plants and their compounds offer a variety of pharmacological actions, such as anticancer therapy, immune regulation, autonomic nervous activation, antipyretic, analgesic, hepato-protection, and antidiabetic properties, among others. Researchers have started to connect a plant's phytochemical constituents to its pharmacological effectiveness, as well as morphological qualities to pharmacological effects. In the future, more coordinated multidimensional research is expected to link botanical and phytochemical features to give specific pharmaceutical effects. More emphasis has been made to Central Nervous System-active, cytoprotective, immunomodulators, and chemotherapeutic plant products in terms of therapeutic potential. (Singh & Sedha, 2018)

## 1.1.A glimpse on historical use of medicinal plants

It's tough to pinpoint the exact time when plants should be used as a medication. Plants were grown as medications roughly 60 000 years ago, according to research. In India, China, and Egypt dating back almost 5000 years, and at least 2500 years in Greece and Central Asia documents about medicinal plants may be found. People have been trying to heal themselves with nature since the dawn of humanity. As the usage of animals was instinctual oh that time, the same instinct was extended to plants. Also, there was a lack of information regarding the causes of the sickness, effective plants for treating it, and how to employ them for that purpose at the time, everything was done on the basis of trial and error. The reasons for the use of certain medicinal plants for the treatment of specific ailments were gradually found over time; as a result, the use of medicinal plants eventually discarded the research model and was limited to the facts. Going back approximately 5000 years, on a Sumerian clay slab from Nagpur, the oldest recorded evidence of the usage of medicinal herbs for medication manufacture was discovered. Going back at least more than 27 centuries BC, Egyptians and Chinese were among the first human beings to use plants as medication based on particular documents. The therapeutic properties of several medicinal plants were also known to ancient Greeks, and Hippocrates, the father of Greek medicine, and Aristotle, Hippocrates' student, employed medicinal plants to treat illnesses. Following that, The School of Medicinal Plants was established by a Greek scientist named Theophrastus. Then, between 75 and 45 BC, Pedanius Dioscorides (who lived in the first century A.D.) published an encyclopedia called De Materia Medica, in which he described 600 therapeutic medicinal plants in the sequence of scientific research on medicinal plants. (Jamshidi-Kia et al., 2018)

*Figure 1: Pedanius Dioscorides and his encyclopedia's one page from "De Materia Medica"*(Marketos et al., 1990; Masic, 2017)

## 1.2 Importance of medicinal plants

Alternative medicine, that is basically the use of plants to obtain a therapeutic goal. Practically, this is widely utilized in all countries, especially in Asian and Western societies. However, the majority of people even now still consider that the only safe and robust treatment is one that comes in a pill form (such as tablets, capsules, etc). Since many tablets or capsules are ingested on a regular basis, many of them are derived from plant chemicals like aspirin, digoxin, paclitaxel, etc. Plants and herbs were used by our forefathers to store and flavor food, relieve any kind of pain, heal headaches, and sometimes even cure illnesses such as a pandemic. The medicinal powers of these plants have been passed down through the generations within and among human communities. Including the treatment of infectious diseases, the biological capabilities of plant species are utilized all over the world for numerous purposes and these are used mainly due to active chemicals formed during biotransformation. Nowadays, many studies are alerting the public about the risk of pathogenic microorganisms that have developed bacterial resistance. Even though information on the antibacterial effectiveness of numerous plants previously considered valid, has been scientifically clarified, many investigations are yet necessary to describe the chemical properties of these plant antimicrobial compounds and the systems involved in bacterial growth inhibition, whether independently or in combination with exposure to pathogens(Hoffman, 2001; R., 2015)

## 1.3.Medicinal Plants in Bangladesh’s Perspective

One of the developing countries is Bangladesh. Most of the people living in rural areas do not use advanced care services because of poor road networks, a shortage of allopathic medical professionals or clinics, the inability to pay for modern medicines, and an age-old reliance on traditional medical providers. (Haque et al., 2015)

As there are plenty of medicinal plants in this region, plants and herbs have been the standard treatment in many tribal areas of Bangladesh. Since ancient times, people all across the world have acknowledged nature and natural medicines. Even before the identification of diverse microorganisms, barks, roots, stems, flowers, seeds, and other components of plants were utilized to treat diseases or infections caused by bacteria. As a result, it's logical to assume that these herbs and plants have enormous therapeutic value and pharmacological effects. (Bardhan et al., 2018) .People like tribal communities in Bangladesh's isolated upland areas depend greatly on natural remedies. Approximately 450 to 500 plants cultivated or present in Bangladesh have been identified as having therapeutic significance. The majority of Bangladesh's medicinal plants are widely employed in the formulation of Unani, Ayurvedic, and Allopathic medicines. In fact, twenty pharmaceutical industries proposed to develop herbal treatments in Bangladesh, acknowledging the good prospect of medicinal plants. The related sectors in Bangladesh need around 6,000 metric tons of medicinal plants each year to prepare traditional medicines. Moreover, nowadays, in Bangladesh, there are a number of laws, regulations, and protocols in place to safeguard environmental capital (medicinal plants). (Motaleb, 2011)

## 1.4.Challenges and overcomes in medicinal plant history

As there are over half a million plants on the planet, most of which still have not been researched in clinical practice, present, and emerging scientific studies can be useful in treating disease. In the case of therapies or exploration, there is a long tradition to the use of medicinal plants; even so, there are numerous challenges, including modifications of plant's materials in various atmospheres, synchronous innovation of synergistic molecules that result in inhibitory action, as well as other abrupt changes in bioactivity, and changes or degradation of bioactivity variation and accumulation. Previously, drug development of biological molecules via plant products and the method of defining the structural patterns of active compounds through extraction was so much complicated and challenging and depending on the nature of the compounds, it took several weeks, months, or even years. But currently, the advancement of scientific instruments including high-performance liquid chromatography (HPLC/MS), liquid chromatography-mass spectrometry (LC/MS), magnetic field, and nuclear magnetic resonance (NMR) have been considerably increasing. (NMR) is a new key advancement in the classification of substances that are extremely rare in their natural habitats. During development, preparation, and harvesting, herbaceous plants are commonly affected by heavy metals contamination and degradation which are two major issues regarding natural medications but nowadays, various instruments can detect these types of metal elements and also help to eliminate them. GAP is a method for assisting in the resolution of many problems by using high-quality, safe, and non-contaminated (raw pharmaceuticals) herbal medications. Ecological environment, production locations, genetics, growth, collection, and quality attributes of trace analysis, macroscopic or microscopic evaluation, analytical detection of active chemicals, and metal element checking are all covered by GAP. For the development of herbal medicines, thus it is essential to increase the efficiency and effectiveness of phytochemical compounds while also exploring further new herbal products. Another difficulty is the depletion of plant species due to the inappropriate application of these materials. Worldwide, approximately 50 000 and 80 000 floral species of plants are being used for pharmacological activities, as per the International Union for Conservation of Nature information. Even, nearly 15 000 species are threatened by rapid depletion of excessive extraction and ecosystem damage, and 20% of its animal sources are diminishing as a result of expanding human communities and inappropriate plant cultivation.

Moreover, many people today use herbal medications as part of their healthcare, still, there are many questions about their efficacy and safety. So, scientific justifications can be translated in order to establish trust for the use of plants in traditional medicine. Although herbal medicines have the potential to revolutionize healthcare, several crucial difficulties must be overcome. One of the most significant issues in this discipline is the lack of correct interpretation of materials and scientific data on plants by researchers all over the world. For this reason, scientists and physicians in both modern and traditional medicine must be trained in the use of plant chemicals in order to ensure effective plant incorporation into a healthcare system. Furthermore, Finally, various problems regarding safety, dosage accuracy, treatment duration, side effects, acute and chronic toxicities, and standardization of herbal medications and natural products must be addressed. (Jamshidi-Kia et al., 2018)

## 1.5. Phytomedicine

Herbal medication having therapeutic and healing characteristics is referred to as phytomedicine. It has existed from the beginning of human society. Herbal medicines are amongst the most demanded basic health care options for almost 3.54 billion people worldwide, according to WHO statistics, and a significant proportion of herbal medicine requires plant extract-derivatives and tinctures, which can also be referred to as "advanced herbal medicine." Phytomedicine, in combination with other healthcare sectors, has modernized and enhanced the foundation of the current healthcare system, and it now holds a significant share of the market. According to some data analyses, from around the world, approximately 35,000 kinds of plants are now used in herbal medicines and recipes. (Srivastava et al., 2018)

In addition, approximately 400 new infectious microorganisms have been discovered throughout 1940, and vaccine development has been tremendously successful for these microorganisms and also for other diseases too. After that, SARS-CoV-2 is a novel human coronavirus that has caused an epidemic outbreak. But there is currently no cure for COVID-19 and it has caused a major danger to worldwide life and the economy. There are so many scientists and experts all across the world who are trying to come up with a cure. Eventually, some strict health strategies have been adopted, including handwashing, masks, and isolation. Also, numerous studies to develop a chemical medication have been made, and various clinical experiments have demonstrated that plant extract preparations in conjunction with other drugs have exhibited positive outcomes. (Sohail et al., 2021)

Plant secondary metabolites, often known as phytochemicals, are metabolic compounds that play a role in defensive mechanisms towards pathogens. Multiple bioactive components, widely categorized as alkaloids, polyphenols, chloroquine, and terpenoids, have been demonstrated to be effective towards new coronaviruses in several in silico, in vivo, in vitro, and clinical investigations conducted across the world and shown positive results. The basic mechanism of action for phytochemicals is to prevent the entry of such viruses by conjugating specific receptor sites in targeted cells and to inhibit the replication cycle of these pathogens through degrading viral polymerases and proteases, which are required for virus assembly. Phytomedicines have also been shown to enhance immunity to new coronaviruses and appeared to be viable choices. So, additional research is required to identify and test all potential targets. (Sohail et al., 2021)

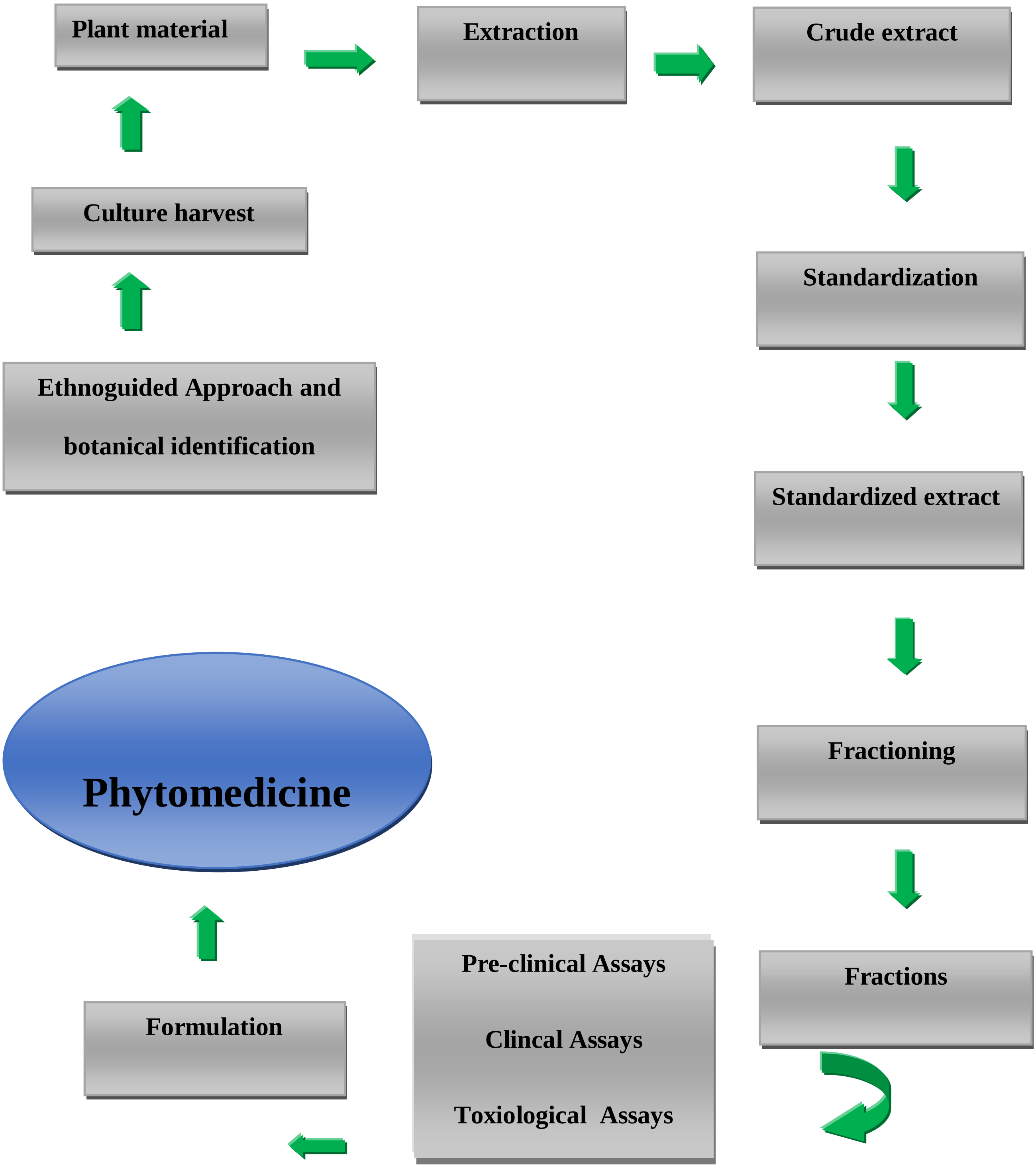


*Figure 2: Development of Phytomedicine*(Ramos Barbosa et al., 2012)

### 1.6. Future of Medicinal Plants

Natural compounds have a good prospect. Plant-derived goods have definitely risen in popularity in recent years. More than 85 percent of people in the Middle East, Latin America, Africa, and Asia depend on conventional medicine, particularly herbal medications, for their health care. Traditional, complementary, and herbal treatments are still used by almost 100 million people in the European Union and up to 90% of the people in other countries. Herbal medicine is becoming increasingly popular. These requirements are mainly influenced by female respondents, who are more concerned about the negative effects of synthetic medications. Also, human resource training can be a major source of research development with the aim of converting from manufacturing to agricultural production. Researchers in the area of medicinal plants are more important than ever before. Various plant species are used as adjuvant therapy in health care systems around the world, both to treat, prevent and preserve health. Though there is substantial experience with plant species in herbal medicine, scientific research and characterization of bioactive plant chemicals and their impacts may one day result in the identification of novel therapeutic value and the manufacturing of natural products. To accomplish this, one of the major studies is required to control the quality of raw substances and preparations in order to validate their usage in the advanced medicine sector. Additionally, experimental research and studies trials are necessary to achieve the benefits of these plants. Moreover, a comprehensive strategy for maintaining these assets should be devised as part of the production of medicine via medicinal plants, along with other things. (Jamshidi-Kia et al., 2018)

## 1.7. Rationale of the study

Medicinal plants play a vital role in the case of new drug development and phytochemicals contain natural compounds in plants that have therapeutic potential by assisting plants in defending themselves against many harmful things. *B. gymnorhiza* is a plant that has a lot of pharmacological activities and impacts the function of various organs. Researchers have done various investigations to learn more about the phytochemical ingredients and pharmacological potential of the plant. It has been found that *B. gymnorhiza* has high antidiarrheal, analgesic, antimicrobial, hepatoprotective, antihyperglycemic, antilipidemic, antihemolytic, antioxidant, and anticancer activities. Furthermore, chemical components extracted from this plant, such as flavonoids, tannins, phenolic compounds, saponins, terpenoids, and many others, enhance its different pharmacological effects. The knowledge of plants' phytochemistry and pharmacology properties are the focus of this review.

## 1.8. Aim of the study

This project paper on the *B. gymnorhiza* as a mangrove plant is carried out in order to combine some vital information regarding its pharmacological and phytochemical activities. This study could help to expand knowledge of this plant and identify new research areas on mangrove plants that could lead to the discovery of novel lead chemicals for future medication development.

## 1.9. Objective of the study

The main objective of this study was-

1. Increase the knowledge on mangrove plants that can be used as medicinal plants of Bangladesh.
2. Getting the information on the plant's features, taxonomy, history, and medicinal use.
3. Documentation of pharmacological and phytochemical study on mangrove plant.
4. Identifying a new research area for mangrove plants.
5. Reference for researchers and academics

# Chapter 2 -Plant Review

## 2.1. *B. gymnorrhiza*

One of the distinctive and significant ecosystems is mangroves, which is made up of a large number of trees-like coastal sea plants that grow along the edges of tropical shorelines throughout the world. Mangrove plants have unique lenticels to convey gases from bare roots at sea level, whereas heavy rain waves enable nutrient intake and seed dissemination, frequently employing highly floating seedlings. And here is the big-leafed, one of the most significant and widely available mangrove species in the Pacific. This is widely distributed in the tropical Pacific region's intertidal zones, from Southeast Asia through southern Japan's Ryukyu Islands, Micronesia and Polynesia (Samoa), and southward to subtropical Australia. This mangrove species can flourish in a wide range of intertidal circumstances such as salt levels ranging from near groundwater to full-strength saltwater, and it can endure flooding and a variety of types of soils. It's hard to isolate this kind of plants' usefulness from the greater contribution served by overall mangrove species. Mangrove forests are the ones that perform critical roles in coastal protection, improving water quality in nearshore areas (particularly over coral reefs), providing space for aquatic species as well as other coastal species, and maintaining aquatic food chains via carbon outwelling. Even though the wood is the most commonly utilized portion of the tree in most of the Pacific, other parts of the tree, such as propagules, leaves, and bark, have been known to have multiple applications in the region. (West & Duke, 2006) .

The *B. gymnorrhiza* tree is a short tree that can reach its height of about 10 meters. This tree grows mainly on the seaward edge of mangrove areas in Bangladesh's Sunderbans forest. Some short prop-roots grow on this tree and the fruits of these trees are kind of spindleshaped and fall to the ground in an upstand position, where they attach themselves to the ground and establish roots. (Zahirul Kabir et al., 2013)

*Figure 3: large-leafed mangrove B. gymnorrhiza*(West & Duke, 2006)

## 2.2. Distribution

This mangrove tree is broadly found in the tropical South and East Africa, Madagascar, Seychelles, and Sri Lanka, and is amongst the most available trees in the tropics. (Zahirul Kabir et al., 2013). It has the natural greatest distribution of overall mangrove species, ranging from the east African coast to Asia to the Ryukyu Islands of southern Japan, across Micronesia and Polynesia (Samoa), as well as southward to subtropical Australia (Queensland, New South Wales, and Western Australia). However, this is more usually located in the central and top coastal areas, instead of the bottom coastal areas or even the outer coastal edge, inside the mangrove habitat. Also, these large-leafed mangroves can be cultivated in direct sunlight or in a variety of shadow conditions. In Australia, 30 percent shade is advised for Bruguiera species. (West & Duke, 2006) In Bangladesh's Sunderbans forest, the tree can be mostly founded one, which includes part of the Khulna Division. The Sunderbans forest is claimed to be the world's biggest mangrove forest. (Zahirul Kabir et al., 2013)

## 2.3. Different names

- Bangladeshi name - Kankra
- Northern Australian name - black mangrove; large-leafed mangrove; orange mangrove
- Andhra Pradesh, Indian name - thuddu ponna or uredi
- Sri Lankan name - malkadol or srikanda
- Kenya, Tanzania, Zanzibar, Mozambique name- muia or mkoko wimbi
- Cambodian name - prasak tooch or Burma mangrove
- Tagalog, the Phillipines name - bakauan
- Sumatra, Indonesian name - putut
- Peninsular malay name - bakau besar
- Pidgin Papua New Guinea name - mangoro
- Singaporean name - tumu merah
- Thais name - pang ka ha sum
- Vietnamese name - vet den (Zahirul Kabir et al., 2013)

## 2.4. Scientific classification

*Table 1: Scientific classification of B. gymnorrhiza*(Zahirul Kabir et al., 2013)

| | |
|---|---|
| **Kingdom** | Plantae |
| **Phylum** | Streptophyta |
| **Order** | Malphigales |
| **Family** | Rhizophoraceae |
| **Genus** | Bruguiera |
| **Species** | *B. gymnorhiza (L.)* |

## 2.5. Botanical description

- **The whole plant of *B. gymnorhiza* :** It is a middle-shaped big tree that can grow to a height of 30–35 m (100–115 ft), however, it is usually much smaller. The most typical diameters are 15–35 cm (6–14 in)(West & Duke, 2006).


*Figure 4:Whole plant of B. gymnorhiza*(Musara et al., 2020)

- **Roots of *B. gymnorhiza:*** The base of *B. gymnorhiza* is upright, with a width of 40-90 cm. (Musara et al., 2020). Large-leafed mangroves are usually single-stemmed plants with small buttresses and distinctive "knee roots," which are parallel roots that often generate above-ground loops, apparently to assist in the exchange of gases for the root systems' subsurface sections. On the coastal border of stands or in salt concentrations environments, it has a smaller height and a more conical appearance. (West & Duke, 2006)

*Figure 5: Roots of B. gymnorhiza*(West & Duke, 2006)

- **The bark of *B. gymnorhiza plant:*** The bark is usually light brownish to grey in color (darker while moist), thicker than 2 cm (0.8 in the), firm, and rugged. Vertical crevices and big flaky lenticels 2 cm (0.8 in) in width distinguish the bark of populations on Hainan Island (China). (West & Duke, 2006)

*Figure 6: Bark of B. gymnorhiza plant*(Fourqurean et al., 2010)

- **Leaves of *B. gymnorhiza* plant**: Leaves are opposite, simple, oval, dark green, and coriaceous (leathery), and clustered in bunches of approximately 12 leaves at the terminals of apical stems. Petioles are 2–4 cm (0.8–1.6 in) long and 5–8 cm (2–3 in) wide. Leaves are 8–22 cm (3–8.5 in) long and 5–8 cm (2–3 in) wide. Leaf-blades are oval to rectangular in shape, measuring around 15 cm (6 in) long and 6 cm (2.4 in) wide, with a sharp apex and a 4 cm (1.6 in) long petiole. Stipules (leaf sheaths) are 4–8 cm (1.6–3.2 in) in length and greenish or yellowish. The apical shoots are approximately 6 cm (2.4 in) in length. *B. gymnorrhiza* plants can be identified from other Bruguiera spp. by their leaf color, size, and form from a distance. The lack of a mucronate leaf tip, longitudinal fold grooves along the blade, and cork wart dots distinguish it from Rhizophora spp. Leaf emergence occurs mostly in the south pole during November to March, and in the northern hemisphere from May to September; if rainfall is minimal during these months, canopy density may suffer significantly. Leaf fall happens primarily during the rainy summer season, which runs from October to March in the south pole and April to September in the northern(West & Duke, 2006).

*Figure 7: Leaves of B. gymnorhiza plant*(West & Duke, 2006)

- **Flower of *B. gymnorhiza* plant:** The flowers are so much beautiful. Single flower buds, placed in axils of the leaves, frequently drooping and set at the first (or occasionally second) stem underneath the apical stalk, make up the inflorescence. When the flower is matured and closed, the measurement is 3.0–3.5 cm (1.2–1.4 in) in length and 1.5–3.5 cm (0.6–1.4 in) in width. Calyxes are normally reddish to almost scarlet, sometimes pale yellow, white, or green, smooth or with grooves above lobe junctures, occasionally ribbed, and have 12–14 lobes that are highly sharp and slender. Its form is pale green and slightly curved, with 3–4 lobes and a length of 20 mm (0.8 in) and a width of 1 mm (0.04 in). Petals are likely to develop over time (one-third of overall length), having hairy external borders, creamy-white when young, becoming orange-brown as they mature, around 15 mm (0.6 in) long and 4 mm (0.16 in) wide, and the number corresponds the number of calyx lobes. Between the lobes, the spike is solitary, straight, and up to 4 mm long. Bristles (3–4) on the ends of petal lobes are 3–4 mm (0.12–0.16 in) long and frequently curly. At maturity, stamens range in color from creamy white to golden brown and are roughly 12 mm (0.5 in) in length. The petiole is smooth, thin, and curved, with a length of 10 mm (0.4 in) and a width of 2–3 mm (0.08–0.12 in). In the southern hemisphere, from April to August, and in the northern hemisphere, from October to February, flowering occurs. (West & Duke, 2006)

*Figure 8: Flower of B. gymnorhiza plant*(Allen & Duke, 2006)

- **Fruit of *B. gymnorhiza* plant**: The internal fertilization nature of the large-leafed mangrove means that it generates seeds that develop on the parent organism. A hypocotyl is a viviparous seedling that serves as a spreading unit. There is no evidence of a fruiting stage. However, a solitary hypocotyl arises from a mature calyx linked to it. At the third to fifth nodes underneath the apical shoot, mature hypocotyls with joined calyx bodies can be found. The hypocotyl is spherical, long, heavyset, dark green, coriaceous, with longitudinal ribbing providing it an angled appearance, a sharply pointed root tip, mature proportions 15–25 cm (6–10 in) length, and around 2 cm (0.8 in) width. After adult propagules drop from mother plants, dead calyces often remain attached. In the south pole, mature hypocotyls fall from January to February, while in the northern hemisphere, matured hypocotyls fall from July to August.

*Figure 9: Fruit of B. gymnorhiza plant* (West & Duke, 2006)

- **Seed of *B. gymnorhiza:*** The large-leafed mangrove, like all Bruguiera plants, is viviparous, indicating it generates seeds concealed in the adult calyx (post-flowering) that grow on the parent plant. Each mature calyx normally produces only one hypocotyl, though twins have been reported on rare instances(West & Duke, 2006).

*Figure 10: Seed of B. gymnorhiza plant*(West & Duke, 2006)

## 2.6. Therapeutic aspects

As we already know, people depend on plants mainly for alternative therapies so it has been found that according to the World Health Organization, *B. gymnorhiza* has been widely utilized for this reason by over 80% of the worldwide people. Wood is the most common application of *B. gymnorhiza*, although other functions include foodstuff, pharmaceuticals, colors, and ecological benefits. The therapeutic effects of *B. gymnorhiza* have been documented in a number of countries, including China, Indonesia, Solomon Islands, Bangladesh, Thailand, and the Indian Sundarbans, as per the ethnomedicinal survey. Moreover, *B. gymnorhiza* has been used for medicinal purposes to treat many different types of ailments/complaints, including diabetes, dysentery, influenza, malaria discomfort, and wounds, among others. However, more clinical research is needed to verify this information. (Musara et al., 2020)

*Table 2: Parts of B. gymnorhiza plant and its Therapeutic applications*(Musara et al., 2020)

| Parts of *B.gymnorhiza* plant | Therapeutic applications |
|---|---|
| **Root** | • Diabetes can be treated<br>• In Central China, this part is used to treat diarrhea<br>• In case of malaria and any kind of burn, this part helps to cure it |
| **Bark** | In Indonesia, Solomon Islands, Cambodia, this part is used to treat-<br>• Fever, diarrhea, diabetes<br>• It also used as an abortifacient to cure burns and<br>• As astringent (which is not very harmful)to cure malaria |

Table 2: Continued

| Parts of *B. gymnorhiza* plant | Therapeutic applications |
|---|---|
| **Stem** | • Seasonal or any viral fever can be treated. |
| **Leaves** | • This helps to treat diarrhea, fever, malaria, burns cuts, wounds, intestinal worms, liver disorders, and tumor inhibitors |
| **Fruit** | • In case of diarrhea and fever, diabetes, pain, burns, intestinal worms, and liver disorders, it is very effective to treat.<br>• Also, it has antiviral effectiveness; used for diarrhea treatment, and also play a vital role in the treatment of shingles and eye diseases |

## 2.7. Uses and Importances

Mangroves are the ones that play an important role in safeguarding and maintaining aquatic food cycles by providing plant substances, that act as a source of nutrition in coastal areas. In this case(Musara et al., 2020)-

- This *B. gymnorhiza* helps to generate highly organic soil habitats by its great fertility that are transferred to surrounding marine ecosystems.

- As *B. gymnorhiza* are dicot type woody bushes or trees, it helps to typically produce specific natural habitats that are suitable for a diverse range of species. They also nurture phytoplankton, zooplankton, and fish communities, as well as provide a hatchery and nursery environment for fish larvae whose adults live in other ecosystems including coral reefs and seagrasses.

- Mangroves of the genus *B. gymnorhiza* play a significant role in coastal stability and safety by holding sediment and driving sea storms and breezes at bay which help to reduce soil degradation and property damage.

- *B. gymnorhiza* has been discovered to have excellent bioremediation capacity as well as the greatest water treatment effectiveness.

- *B. gymnorhiza* species are also essential for carbon capture and storage, as well as serving as fish breeding places and beautification. For example, budding hypocotyls are produced commercially as aesthetic plants in Japanese tourist shops.

- The bark of the *B. gymnorhiza* plant is used to synthesize pigments that vary from red-brown to black, and it has a high tannin content, although it prefers to color leather significantly if it is harvested after each growing season.

- The flowers of *B. gymnorhiza* are used in body adornment and garlands, while the knee roots are used to make fragrances.

- *B. gymnorhiza* wood is recognized because of is hydrophobic, borer-resistant, robust, and practically indestructible, making it a highly desired wood.

- On some islands, the wood is also utilized to build blades and oars for propelling boats and canoes. In some areas (the Andaman Islands), the wood is also used for furniture, fishing stakes, spears, transmission, and telephone poles, and is likely to be durable when in close contact with the earth.

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# Chapter 3 –Phytochemical compounds and their activities

## 3.1. Phytochemical compounds

Phytochemicals (Greek word phyto, which means "plant") are pharmacologically active which are natural sources of chemical compounds that are commonly found in plants. They have beneficial effects on human health that go beyond those provided by macronutrients and micronutrients. Phytochemicals can be found in a variety of plant parts, including the roots, plant metabolites. They are molecules with biological features such as antioxidant properties, antimicrobial properties, detoxification enzyme modulation, immune system activation properties, platelet aggregation reduction properties, hormone metabolism regulation properties, and anticancer effects. There are about a thousand recognized phytochemicals and many more still undiscovered phytochemicals(Costa et al., 1999; Hasler & Blumberg, 1999; Kris-Etherton et al., 2002). Antioxidant property, enzymatic modulation, immune system stimulation, hormone metabolism modulation, antibacterial and antiviral effects, involvement with DNA replication, and physical action (some phytoconstituents attach physically to cell membranes, blocking pathogen adhesion to human cell membranes) are just a few of the mechanisms that phytochemicals can have in the body. (Njerua et al., 2013)

Various chemical agents, as well as particular tests for individual phytochemicals, are developed. These tests are all qualitative, hence they are referred to as phytochemical screening. (Sharma et al., 2020)Alkaloids, glycosides, flavonoids, saponins, tannin, gums, and terpenoids were detected in the specimens through qualitative phytochemical testing. Dragendroff's, Mayer's, Hager's, and Wagner's techniques were used to identify alkaloids. Flavonoids were identified through lead acetate, alkaline reagent, ferric chloride, and ammonia assays. To detect glycosides, researchers used Legal's assay, Molisch's experiment, Keller-test, Kiliani's, and Borntrager's experiment. The ferric chloride, potassium hydroxide, potassium dichromate, and lead acetate assays were used to detect tannin. To determine the presence of terpenoids and saponins, the Salkowski assay and the froth test were utilized. (Mahmud et al., 2017) .According to their function in plant metabolism, phytochemicals are now characterized as primary or secondary constituents. Sugars, amino acids, proteins, nucleic acid purines, pyrimidines, chlorophyll, and other primary components are among them. Alkaloids, terpenes, flavonoids, lignans, plant steroids, curcumins, saponins, phenolics, flavonoids, and glucosides are examples of secondary components(Kurmukov, 2013).

*Table 3: Phytochemicals derived from plants and their mechanism of action*(Tiwari Prashant, Kumar Bimlesh, Kaur Mandeep, Kaur Gurpeet, 2017)

| Phytochemicals | Activity | Mechanism of action |
|---|---|---|
| Quinones | Antimicrobial | • Inhibits enzymes via binding to adhesins, forming a complex with the cell wall |
| Flavonoids | Antimicrobial<br>Antidiarrhoeal | • It forms a complex with the cell wall and binds to adhesins.<br>• Autocoids and prostaglandins are inhibited.<br>• Spasmogen-induced contractions are inhibited.<br>• Activates the restoration of normal water transport throughout the mucosal cells.<br>• Suppress acetylcholine release in the gastrointestinal tract. |

Table 3: Continued

| Phytochemicals | Activity | Mechanism of action |
|---|---|---|
| Polyphenols and Tannins | Antimicrobial<br><br>Antidiarrhoeal<br><br>Anthelmintic | • Works by binding to adhesins, inhibits enzymes, deprives a substrate, forms a complex with the cell wall, disrupts membranes, and complexes metal ions<br>• Inhibits the adherence of the B subunit of heat-labile enterotoxin to GM1, and promotes restoration of deranged water movement throughout the mucosal cells and reduction of intestinal transit leading to the suppression of heat-labile enterotoxin-induced diarrhea, astringent action.<br>• Increases the quantity of digestible protein availability to animals by building protein complexes in the stomach, interacts with energy synthesis by uncoupling oxidative phosphorylation, and lowers G.I. metabolism. |
| Terpenoids and essential oils | Antimicrobial<br>Antidiarrhoeal | • Membrane rupturing<br>• Autocoids and prostaglandins are inhibited by this. |
| Alkaloids | Antimicrobial<br>Antidiarrhoeal<br>Anthelmintic | • Works by interfering with parasite cell walls and DNA. Autocoids and prostaglandins are inhibited.<br>• Anti-oxidant properties limit nitrate production, which is important for protein synthesis; inhibit sucrose transport from the stomach to the small intestine, reducing glucose support for the helminths; and act on the central nervous system, producing paralysis. |
| Lectins and Polypeptides | Antiviral | • Forms disulfide bridges and prevents viral fusion or adsorption. |

Table 3: Continued

| Phytochemicals | Activity | Mechanism of action |
|---|---|---|
| Glycosides | Antidiarrhoeal | • Autocoids and prostaglandins are inhibited by this. |
| Saponins | Antidiarrhoeal<br>Anticancer<br>Anthelmintic | • In vitro, it suppresses the release of histamine.<br>• It has the ability to permeate membranes. Causes tegument vacuolization and disintegration. |
| Steroids | Antidiarrhoeal | • IncreaseNa+ and water absorption in the intestine. |

*B. gymnorhiza* has shown the presence of some phytochemical compounds, including phenolic compounds, flavonoids, saponins, tannins, phytosterols, and terpenoids which are discussed below:

### 3.1.1. Phenolic compounds :

Phenolic phytochemicals are the most abundant and extensively dispersed phytochemicals in the plant kingdom. Flavonoids, phenolic acids, and polyphenols are the three most significant types of dietary phenolics. Phenolics are a type of chemical compound that has a hydroxyl group (-OH) that is directly linked to an aromatic hydrocarbon group. The basic class of this category of natural chemicals is phenol (C6H5OH). They play a crucial function in defense. These chemicals are a well-known class of secondary metabolites with a broad range of pharmacological effects The antioxidant properties of phenolics are essential in determining their role as protective agents against free radical-mediated disease states, and their antioxidant properties are significant in determining their role as protective agents against free radical-mediated disease processes.(Egamberdieva et al., 2016; Kurmukov, 2013)

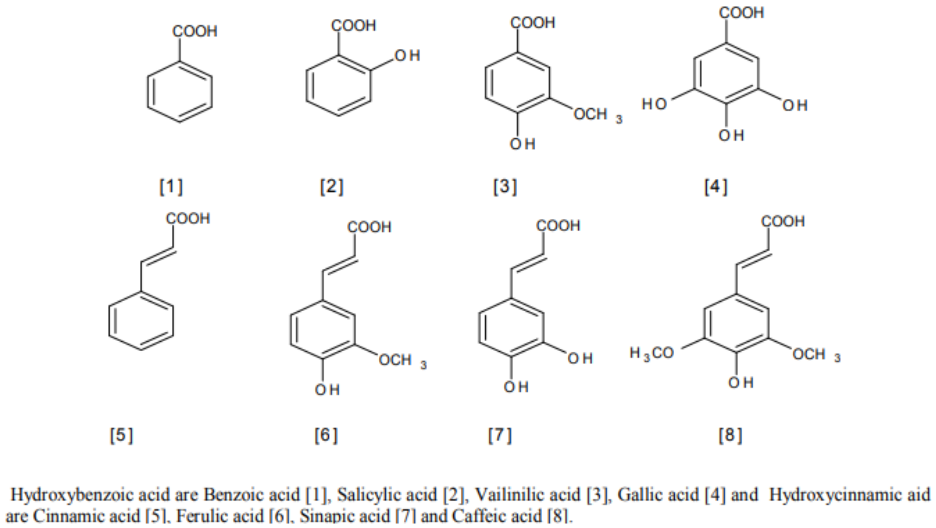
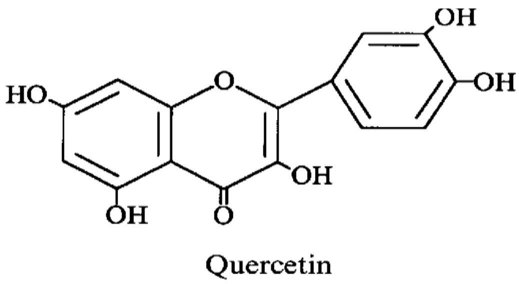



*Figure 11: Structure of phenolic Compounds derived from B. gymnorhiza* (Kurmukov, 2013)

### 3.1.2. Flavonoids

A class of plant secondary metabolites with varied phenolic structures in their molecular system are extensively dispersed in plants. (Egamberdieva et al., 2016). They are phenolic and water-soluble structural derivatives of flavones that contain conjugated aromatic systems and are commonly attached to sugar(s) as glycosides(Harborne, 1998). They act as anti-oxidants, thereby guarding against degenerative diseases. Flavonoids like quercetin (QU) act as chain-breaking antioxidants, preventing macrophages and metal ions like copper from oxidizing low-density lipoprotein. This helps to reduce oxidative stress. Additionally, they function as anti-allergens, anti-inflammatory, and trigger phase two enzymes that remove mutagens and carcinogens, making them "nature's biological modifiers" They also work as antimicrobials by complexing extracellular and soluble proteins, as well as the cell wall of bacteria. Microbial membranes may be disrupted by more lipophilic flavonoids. Surfaceexposed adhesins, cell wall polypeptides, and membrane-bound enzymes are all potential targets on microbial cells. Others, such as catechins(CH) found in oolong green tea, block bacterial glucosyltransferases and inhibit the growth of bacterial toxins (such as cholera toxin). Flavonoids have also been shown to improve coronary flow, lower myocardial oxygen consumption, and lower blood pressure. (Njerua et al., 2013)



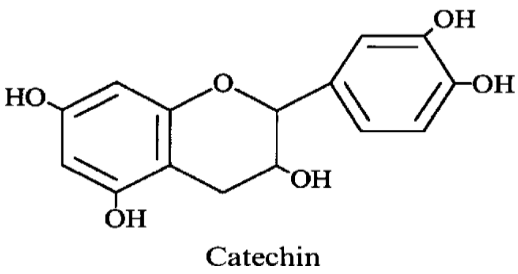




*Figure 12: Flavonoids derived from B. gymnorhiza*(Paganga et al., 1996)

### 3.1.3. Saponins

Saponins are a class of secondary metabolites that can be identified across the plant world. In an aqueous phase like soap, they create a stable foam, thus the name "saponin." Saponins are a chemical field that incorporates glycosylated steroids, triterpenoids, and steroid alkaloids. (Rahman et al., 2011) They have a broad range of biological functions, such as stimulating the respiratory system as an expectorant and thus cough activity. They have also anti-protozoal action, producing cell lysis by interacting with cholesterol in protozoal cell membranes, for example. Yucca saponins are efficient against Giardia lamblia, a protozoan. By functioning as adjuvants, they work as vaccine promoters. Anti-inflammatory, emetic, antiviral, antifungal, insecticidal, molluscicidal, piscidal, and antibacterial properties are all present in them(Njerua et al., 2013). The bactericidal effects are mediated via the saponin's membranolytic capabilities along with a reduction in the extracellular medium's surface tension(Al-Bayati & Al-Mola, 2008). They are important economically as a source of low-cost, eco-friendly detergents and cosmetics. Additionally, some saponins, such as Radix Notoginseng, have been shown to improve coronary artery blood flow, prevent platelet aggregation, and reduce oxygen consumption by heart muscles. Anti-oedema, antitussive, purgative, and immunoregulatory activities are also present (Njerua et al., 2013)

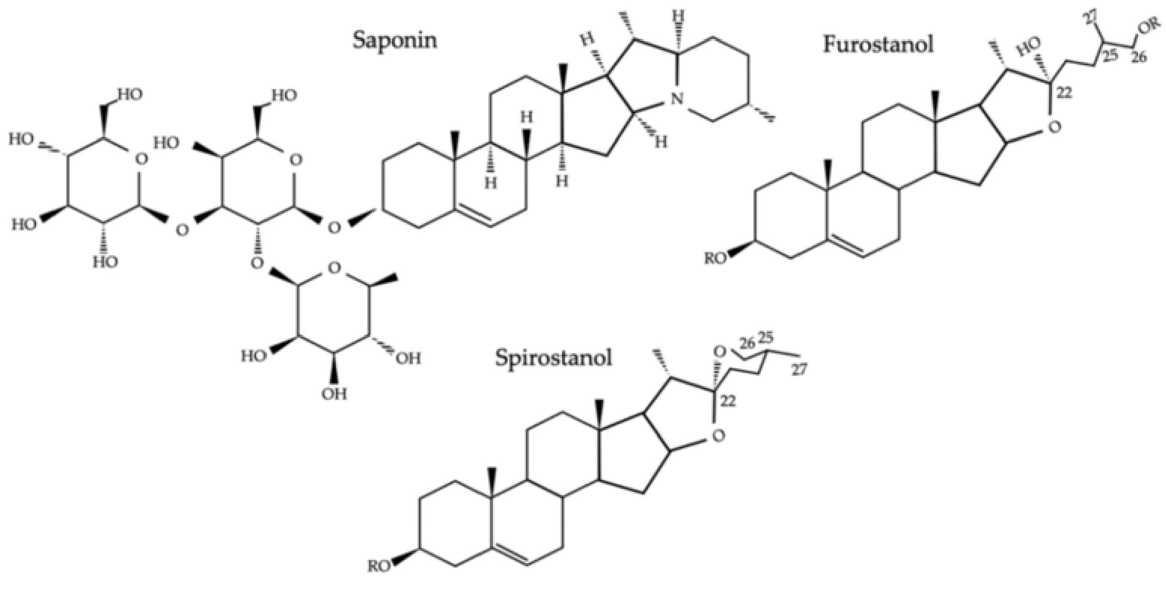



*Figure 13:Basic Saponins* (Ku-Vera et al., 2020)

### 3.1.4. Tannins

Tannins are a heterogeneous class of high molecular weight polyphenolic chemicals that can form reversible and irreversible complexes with proteins (primarily), polysaccharides (cellulose, hemicellulose, pectin, etc.), alkaloids, nucleic acids, minerals, and other substances(B. & I., 1992; Schofield et al., 2001; Van Soest, 2019). As they are astringent, bitter plant polyphenols in nature, they attach to proteins and cause them to precipitate or shrink. They also play a significant physiological role as antioxidants by scavenging free radicals, chelating metal complexes, inhibiting prooxidative enzymes, and preventing lipid peroxidation. Tannins also help to block tumor progression by triggering apoptosis and suppressing carcinogen mutagenicity. They're also anti-inflammatory and molluscicidal, which makes them useful in the fight against schistosomiasis. They have also anti-diarrheal, anti-septic, anti-fungal, anti-parasitic, and anti-irritant properties. Moreover, these tannins are used to stop bleeding, heal wounds, and improve vascular health by decreasing peptides that harden arteries. They also have a role in the economic development in the leather sector by tanning leathers. (Njerua et al., 2013)

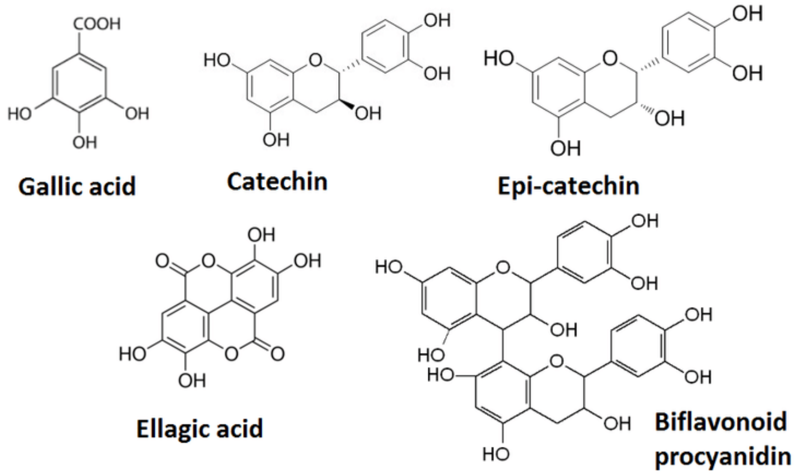
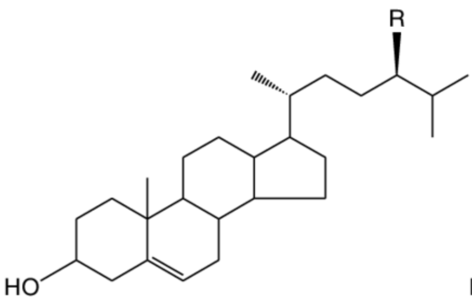


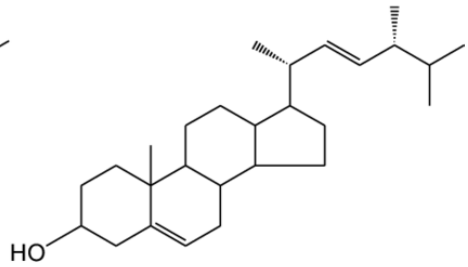

*Figure 14: Tannins derived from B. gymnorhiza* (Multia, 2018)

## 3.1.5. Phytosteroids

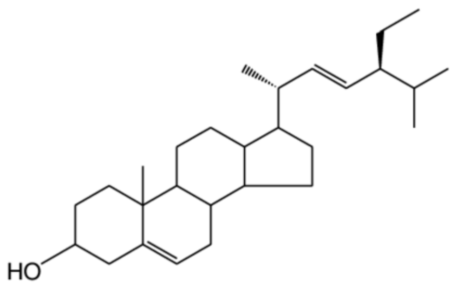
Plant steroids are known as phytosterols which have a fundamental ring structure with animal steroids, but their chemical groups are connected to the primary ring in various locations, therefore they are not similar. They're mostly used to treat fertility problems including venereal illnesses, as well as to enhance fertility in women and libido in men. Moreover, these are also recommended during pregnancy to promote a smooth delivery. Phytosterols have also antimicrobial, analgesic, and anti-inflammatory properties. They're used to treat gastrointestinal reduce the levels of cholesterol in the blood and have also been shown to be effective inhibitors of macrophage activation, preventing the generation of pro-inflammatory cytokines and LPS-induced death. Moreover, they could be used as immunosuppressive drugs, particularly physalins. (Njerua et al., 2013)



1. Cholesterol (R = H)
Campesterol (R = $CH_3$)
β-Sitosterol (R = $C_2H_3$)



2. Ergosterol

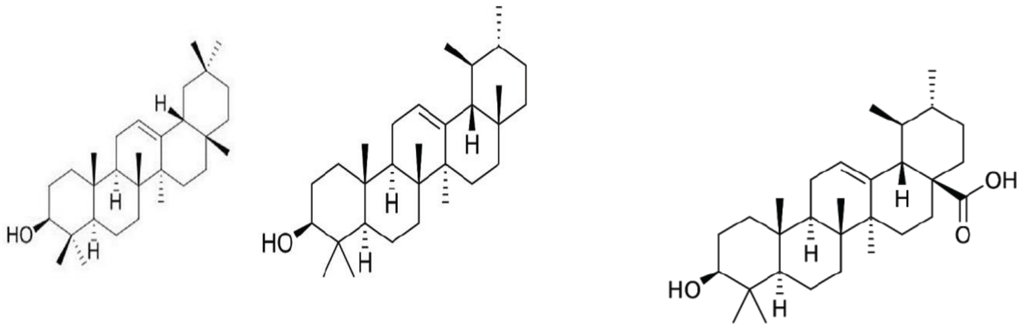


3. Stigmasterol

*Figure 15: Phytosterols derived from B. gymnorhiza*(Wang et al., 1964)

### 3.1.6. Terpenoids

Terpenoids are a group of organic compounds generated from isoprene units with five carbons. Several terpenoids contain multicyclic structures with functional groups and basic carbon structures that vary from one another. Terpenes are found throughout nature, particularly in plants as essential oil components. The hydrocarbon isoprene, CH2=C(CH3)-CH=CH2, is their key part. Terpene hydrocarbons are categorized as per the number of isoprene units in their chemical formula (C5H8). (Kurmukov, 2013). They contain antibacterial, antifungal, antiviral, anti-protozoan, anti-allergen, immune-boosting, and antineoplastic properties. These phytochemicals have the ability to penetrate cell membranes, allowing them to interact with intracellular targets required for antibacterial activity. They are also used to treat epilepsy, as well as to treat colds, influenza, cough, and acute bronchitis. (Njerua et al., 2013)




Name:Beta-amyrin — Molecular formular: $C_{30}H_{50}O$

Name: Alpha-amyrin — Molecular formular: $C_{30}H_{50}O$

Name: Ursolic acid — Molecular formular: $C_{30}H_{48}O_3$

*Figure 16: Terpenoids derived from B. gymnorhiza* (Musara et al., 2020)

The following list is the significant phytochemical compounds identified from various portions of the *B. gymnorrhiza*:

*Table 4: Phytochemical compounds identified from various portions of the B.  gymnorrhiza(*Nebula et al., 2013)

| Plant parts | Phytochemicals | Active components |
|---|---|---|
| Leaves | Triterpenoids | Betulin<br>oleanolic acid<br>β-amyrin<br>ursolic acid<br>α-amyrin |
| | Triterpene alcohol | gymnorhizol (3-epi-δ-amyrin) |
| | Fatty acids | linoleic acid<br>linolenic acid<br>palmitic acid |
| | Sterols | cholesterol<br>Campesterol<br>stigmaste-7-en-3β-ol<br>stigmasterol |
| | Flavonoids | Gramrione (4',5',7-trihydroxy-3',5-dimethoxy flavone) |

Table 4: Continued

| Plant parts | Phytochemicals | Active components |
|---|---|---|
| Flowers | Triterpenoids | bruguierin A<br>bruguierin B<br>bruguierin C |
| Bark | Steroids<br><br><br>Diterpenoids | 3-O-α-L-rhamnopyranosyl-(+)-catechin-(4α→2)phloroglucinol<br><br><br>steviol |
| Stem | Diterpenoids | 13,16,17-trihydroxy-ent-9(11)-kaurene-19-oic acid<br>13-hydroxy-16-ent-kauren-19-al<br>16,17-dihy-droxy-ent-9(11)-kaurene-19-al |
| Stem | Diterpenoids | 16,17-dihydroxy-ent-9(11)-kauren-19-oic acid<br>16-ent-kaurene-13,19-diol<br>16-ent-kauren-19-ol<br>16H-17,19-ent-kauranediol<br>16H-17-hydroxy-ent-kauran-19-oic acid<br>17-chloro-13,16-dihydroxy-ent-kauran-19-al<br>15(S)-isopimar-7-en-15,16-diol<br>(4R,5S,8R,9R,10S,13S)-ent-17-hydroxy-16-oxobeyeran-19-al |

Table 4: Continued

| Plant parts | Phytochemicals | Active components |
|---|---|---|
| Root | Diterpenoids | ent-8(14)-pimarene-1α,15R,16-triol |
| Branch | Aromatic compounds | 2,3-dimethoxy-5-propylphenol |
| Whole plant | Polydisulfide | Gymnorrhizol |
| | Tannins | catechin-3-O-rhamnoside |

# Chapter 4-Pharmacological Activities

There are different pharmacological activities of *B. gymnorrhiza* that has been discovered till now are explained below:

## 4.1. Antidiarrheal activity

Castor oil-induced diarrhea in mice was used to analyze the antidiarrheal efficacy of *B. gymnorrhiza (L.)* extract. Inhibition of intestinal Na+, K+-ATPase activity to decrease adequate fluid absorption, stimulation of adenylate cyclase or mucosal cAMP-mediated active release, activation of prostaglandin formation, platelet-activating component, and, most recently, nitric oxide have all been suggested to demonstrate the diarrheal impact of castor oil. Castor oil, on the other hand, combines with bile and pancreatic enzymes and releases ricinoleic acid from triglycerides when taken orally. The majority of ricinolic acid persists in the intestinal, where it has an absorbent or secretory effect. In the lumen of the intestine, ricinolic acid rapidly released forms of ricinoleate salts with sodium and potassium. In general, ricinoleate salts activate adenyl cyclase or release prostaglandin in the intestinal epithelium. The extract extended the latent time and lowered the frequency of defecation and also the overall number of stool contents. In this case, the methanol roots extract of *B. gymnorrhiza* reduced castor oil-induced diarrhea in the test. Moreover, flavonoids found in the plant extract have been shown to prevent the production of autacoids and prostaglandins, hence suppressing castor oil-induced motility and secretion. The extract's antidiarrhea effectiveness could potentially be related to denatured proteins producing protein tannates, which strengthen the intestinal mucosa and limit secretion. Based on the findings of castor oil-induced diarrhea, the extract appears to have antidiarrheal properties(Rahman et al., 2011).

## 4.2. Analgesic activity:

Without adversely impacting consciousness, an analgesic effectively helps relieve through acting on the central nervous system (CNS) or peripheral pain mechanisms. Acetic acid is a pain stimulant, and intraperitoneal treatment of 0.7 percent acetic acid promotes regional inflammation in mice, resulting in body contractions known as 'writhing.' The action of phospholipase Az and other acyl hydrolases triggers the production of free arachidonic acid from tissue phospholipid in response to a pain stimulation(Uddin & Shilpi, 2006).

The acetic acid-induced writhing technique, which is the most sensitive and well-established method for evaluating analgesia, was used to test the analgesic effect of this plant's extracts. Only a few analgesics have been isolated from plants, necessitating further research to discover further analgesics from natural sources. Higher amounts of local endogenous chemicals, PGE2, PGF2α, and lipoxygenase all are generated from eicosanoids throughout the peritoneal fluid have been referred to as the pain sensations due to intraperitoneal acetic acid injection. As the quantity of the extracts was allowed to raise, the writhing inhibition in mice increased. According to the results of this investigation, stem extracts were more effective than leaf extracts at 250 and 500 mg per kg body weight, since the former induced significant writhing inhibition that was comparable to conventional diclofenac sodium. It is usually recognized that analgesic activity is mediated by a variety of flavonoids, alkaloids,

and steroids. In addition, some of the HPLC analysis revealed polyphenolic components like (+)-catechin, ellagic acid, and vanillin, which have previously been shown to have an analgesic effect. The presence of slightly more polyphenols in stem extract, as well as their synergistic activity, explain that it is more potent as an analgesic agent than other extracts(Mahmud et al., 2017).

*Figure 17: Acetic acid given intraperitoneally and its writing impact on mice(Bhattacharya et al., 2017; Sham Bhat et al., 2015)*

## 4.3. Antimicrobial Activity

There is a large set of data that medicinal plants are highly beneficial in the management of infectious diseases. The plants have a great deal of potential as a source of new antimicrobials. Plant derivatives, such as phytochemicals, have been used to treat a variety of infectious diseases and have shown promising antibacterial activity against a number of human infections(Khameneh et al., 2019). *B. gymnorhiza* extracts in methanol, ethanol, and chloroform demonstrated antibacterial activity, with the ethanol extract having the strongest inhibitory impact against the main bacterial pathogens utilized in the study. As a result, the plant was active against the microbes. In a disc diffusion assay, the pericarp, exocarp, endocarp, and leaves of the *B. gymnorhiza* plant showed antibacterial action against common bacterial pathogens (both Gram-positive and Gram-negative bacteria). The researchers also discovered that n-hexane extracts of several components of this plant had higher antibacterial activity than water extract(Musara et al., 2020).

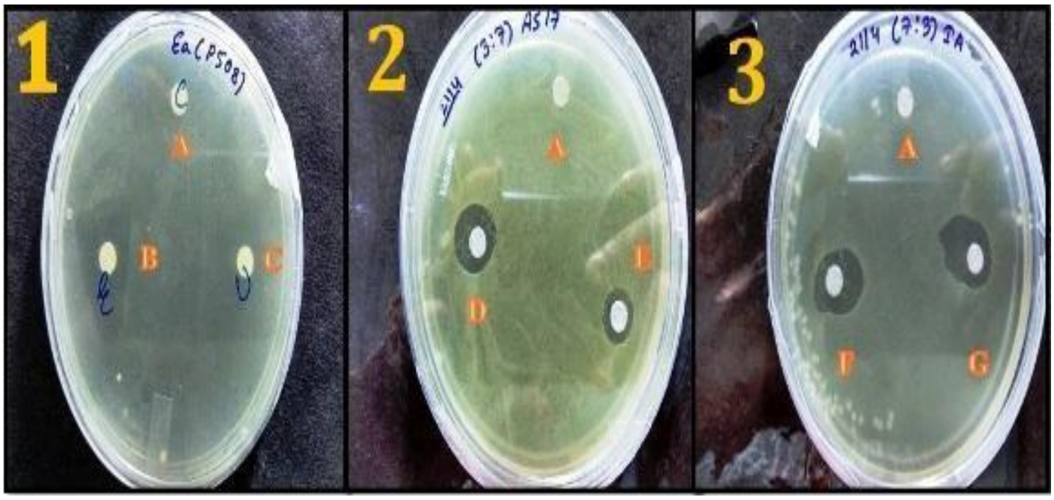



*Figure 18: Antimicrobial test of different B. gymnorhiza extracts through disc diffusion method(Roy et al., 2018)*

## 4.4. Hepatoprotective activity

Hepatic damage is defined by a steady progression from steatosis to chronic hepatitis, fibrosis, cirrhosis, and hepatocellular cancer in the majority of cases. Plant-derived antioxidants, especially polyphenols, have been linked to oxidative stress resistance and hepatoprotection. In addition, mangroves are a significant source of new chemicals with strong antioxidant capabilities. The leaves of *B. gymnorrhiza L.* were found to be high in gallic acid, quercetin, and coumarin, and there is a great deal of evidence to back up its antioxidant and hepatoprotective properties. As per the study, the hepatoprotective efficacy of *B. gymnorhiza* of hydroethanolic extract of leaves was assessed in Dgalactosamine (GalN), and it caused hepatitis in rats. The extraction was given to the rats orally at certain doses for a few days. The leaves of *B. gymnorhiza* provided an amount of drug protection against GalN-induced hepatitis in rats in vivo experiments. GalN is a hepatotoxin that is caused by a deficiency in uridine diphosphate (UDP)glucose or UDPgalactose, which inhibits metabolic activity in hepatocytes or disrupts the mitochondrial membrane, allowing cytochrome C to be discharged from hepatocytes through oxidative stress. The leaking of aminotransferases and alkaline phosphatase enzymes from hepatocytes into blood was caused by these alterations, and these enzymes have become recognized sensitive markers for hepatic damage. The fact that serum levels of AST, ALT, and alkaline phosphatase are greatly decreased after *B. gymnorrhiza L*. administration demonstrates that it has a stabilizing/protective effect on the hepatocyte cell membrane. Moreover, due to its significant antioxidant characteristics, *B. gymnorrhiza L*. therapy lowers the number of lipid peroxides. Caused by the accumulation of hydrogen peroxides in the liver tissues, any decrease in tissue catalase enzymatic activity might have a number of negative consequences. Additionally, decreased GSH works as a free radical scavenger and helps in the recovery of free radical-induced cellular damage. Reduced GSH and catalase levels have been suggested to be a marker of oxidative stress in GalN-induced hepatitis. The restoration of both catalase and GSH in rat liver tissues was dosage-dependent and substantial, indicating that *B. gymnorrhiza L*. may have anti-oxidant properties. Thus, polyphenols found in *B. gymnorrhiza L*. leaves have antioxidant properties and may be used to treat hepatic damage, according to some studies (Sur et al., 2016).

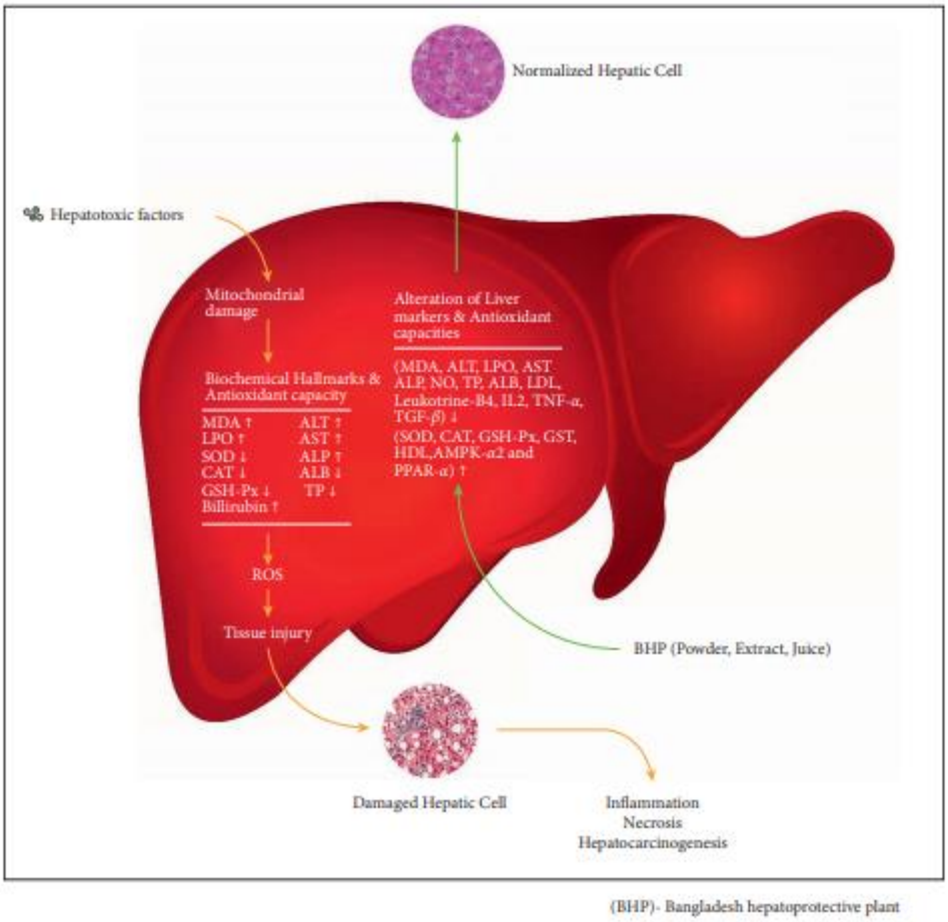



*Figure 19: Effects of hepatotoxic substances and hepatoprotective plants(Rouf et al., 2021)*

## 4.5. Anti-diabetic and Antihyperlipidemic activity

The anti-hyperglycemic activity of an ethanol extract of *B. gymnorhiza* bark was tested in diabetic rats produced with streptozotocin (STZ). Oral ethanolic extract (400 mg/kg body weight) was given for 21 days in a row. The STZ-induced diabetic rats treated with the extracts for 21 days had a considerable drop in blood glucose levels, which was comparable to the conventional medication glibenclamide (0.5 mg/kg). As a result, the extracts brought the rats' blood glucose levels back to normal. There was also a major decrease found in total cholesterol, triglycerides, very-low-density lipoprotein, and low-density lipoprotein(LDL) in diabetic rats, as well as a rise in high-density lipoprotein. The existence of several effective antidiabetic active components, which generated an antihyperglycemic impact in diabetic rats, was considered to be responsible for the plant extract's potent anti-diabetic and anti-hyperlipidemic actions. As a result, more research is needed to isolate the plant's active compounds and optimize them for potency. Similarly, both prepared and raw *B. gymnorhiza* have been shown to have efficacy against type 2 diabetes, with the latter having a substantial insulin-mimetic impact(Balagani, 2021; Sachithanandam et al., 2019; Tiralongo et al., 2011).

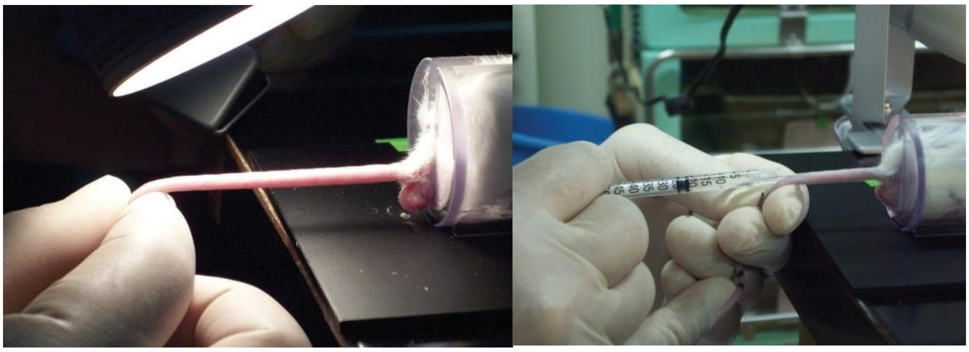


*Figure 20:Injecting STZ solution through the tail vein(Sakata et al., 2012)*

## 4.6. Antihemolytic activity

RBCs(Red blood cells) are the most frequent cells in the human body, each having its own biological and morphological properties. Due to their redox-active oxygen transportation property, hemoglobins and polyunsaturated fatty acids (PUFA) specifically target erythrocytes. For this reason, oxidation mutilates RBCs membrane lipids and proteins during hemolysis. A variety of conditions lead to erythrocyte mutilation, including inadequacies in erythrocyte antioxidant coordination, radiation, excessive levels of metal complexes, oxidative medications, and hemoglobinopathies, among others. Whenever red cells are introduced to toxins like hydrogen peroxide, hemolysis develops at a fast rate. *B. gymnorrhiza* has a stronger anti-hemolytic action, according to some research. When the concentration of extracts and standards increased, erythrocyte lysis decreased in all cases. The hemolysis-prevention activity of *B. gymnorrhiza* was demonstrated(M.A. Ebrahimzadeh et al., 2009; Hamidi & Tajerzadeh, 2003; Naim et al., 2002).

## 4.7. Antioxidant activity

Local metabolic activities mediated by redox enzymes help to produce reactive derivatives of oxygen, that is referred to as reactive oxygen species (ROS). For ensuring a healthy balance, our bodies use antioxidants to neutralize the presence of ROS as a natural defensive response. Yet, in other circumstances, the balance is disturbed by an excess of reactive oxygen species (ROS) and an inadequate antioxidant defense mechanism, resulting in the onset of chronic diseases such as cancer, neurological and cardiovascular diseases, inflammatory disorders, and diabetes. As a result, there is a strong requirement for antioxidants in the form of dietary supplements. In this regard, researchers used some separate mechanisms to analyze the extracts for possible antioxidant properties. Those are radical quenching, reducing potential, metal chelating, etc. Using some tests, the antioxidant capacity of methanolic and ethyl acetate extracts of different plant sections of *B. gymnorhiza* (leaves, twigs, roots, and fruits)was measured as per(Chandrasekaran et al., 2017; Davalli et al., 2016; Mohammad Ali Ebrahimzadeh et al., 2008)study, and found that the methanolic extracts had a higher amount of antioxidant capacity than the ethyl acetate extracts, according to the data

*Table 5: Assays of antioxidant activity*

| **Assays** | **Extracts used** | **Dose** | **In-vivo/ In-vitro screening** | **Statistical analysis** | **Findings** |
|---|---|---|---|---|---|
| DPPH radical scavenging activity test done by(Haq et al., 2011) | 1. Methanolic extract of leaves and bark<br>2. Ethanolic extract of leaves and bark<br>3. Chloroform extract<br>4. Ascorbic acid as control | plant extract(5 mg/ml) mixed with DPPH at an 8 mg/ml. | In-vitro screening | 1. The data were analyzed by one-way ANOVA<br>2. Considered significant values are $p < 0.05$ | 1. Ethanolic extracts of barks had the maximum scavenging activity than other extracts excluding methanolic extracts of barks.<br>2. chloroform extracts of leaves had minimum scavenging. |
| Reducing power test by(Mahmud et al., 2017) | Ethanolic extract of stem and leaves | 10, 20, 40, 60, 80, and 100 g/ mL, | In-vitro screening | 1. ANOVA and Dunnett's test used for analysis<br>2. The data was presented in the form of mean values and standard deviations. | The outcome confirmed some of the scavenging activity. |

Table 5: Continued

| Assays | Extracts used | Dose | In-vivo/ In-vitro screening | Statistical analysis | Findings |
|---|---|---|---|---|---|
| Superoxide dismutase (SOD) test result(Haq et al., 2011) | Bark and leaves of plant extracts treated with ethanol, chloroform, and methanol<br><br>butylated hydroxyanisole (BHA) as control | 1. A blank-1 mixture of working solution (200 µl) and enzyme solution (20 µl) and 20 µl $ddH_20$ water,<br>2.Blank2- a mixture of a working solution of 200µ l and 20µ l of diluted buffer with a plant extract of 20 µl.<br>3.Blank-3 - same way as blank -2, but the plant extract was used in place of 20 µl of ddH2O. | In-vitro screening | 1. The data were analyzed by one-way ANOVA<br>2. Considered significant values are $p< 0.05$ | 1. The result revealed that ethanol extracts of leaves and barks performed significantly better than BHA in SOD assays.<br><br>2. The high phenolic content of the crude extracts B. gymnorrhiza could be the reason. |

Table 5: Continued

| Assays | Extracts used | Dose | In-vivo/ In-vitro screening | Statistical analysis | Findings |
|---|---|---|---|---|---|
| Nitric oxide radical scavenging test by (Mahmud et al., 2017) | Stem and leaves of plant extracts treated with ethanol and methanol | | In-vitro screening | 1. ANOVA and Dunnett's test were used for analysis 2. The data was presented in the form of mean values and standard deviations. | The antioxidant ability of extracts was determined by their phenolic content. |
| Hydrogen peroxide scavenging test by (Mahmud et al., 2017) | Stem and leaves of plant extracts treated with ethanol and methanol | | In-vitro screening | 1. ANOVA and Dunnett's test used for analysis 2. Considered significant values are $p< 0.05$ 3. The data was presented in the form of mean values and standard deviations. | The antioxidant ability of extracts was determined by their phenolic content. |

## 4.8. Anticancer Activity

Cancer is one of the significant health diseases in both industrialized and developing countries. It is one of the world's top causes of death., Cancer killed 12.5 percent of the population in 2004 as per World Health Organization data. It is defined by unregulated and irregular cell proliferation in the human body, which results in malignant cell tumors that have the ability to spread. Lack of physical activity, genetics, an inadequate diet, and different environmental conditions are all possible causes of cancer. A number of chemical compounds are administered to cancer patients, but their toxicity makes them inappropriate for use. Several cancer research investigations have been carried out employing traditional medicinal herbs in the hopes of discovering novel therapeutic medicines that do not have the toxic side effects associated with the current chemotherapy drug. Medicinal herbs have anticancer potential due to their immunomodulatory and antioxidant qualities. These antioxidant phytochemicals effectively protect cells from oxidative stress(Akindele et al., 2015; Bhanot et al., 2011; Kathiresan et al., 2006; Madhuri & Pandey, 2009).

The NF-kB luciferase experiments revealed the activity of *B. gymnorhiza* extracts (petroleum ether, CHCl3, Et2OAC, and MeOH) in combination with bruguiesulfurol, bruguierol, and isobrugierol derived from the plant's flowers. Though, there is insufficient information on this plant's anticancer capabilities; yet, based on the observations, it may be assumed that *B. gymnorhiza* has cancer chemo-preventative action; therefore, more research into the plant's anticancer characteristics is needed(Homhual et al., 2006)

# Chapter 5-Discussion

Plant-derived compounds have currently attracted a lot of attention due to their wide range of functions. Traditional medicines, modern medications, health supplements, food products, herbal products, biopharmaceuticals, and chemical entities for synthesized medicines are all found in medicinal plants(Khatun & Ruma, 2018). Till now, it has been reported that mangrove species have an ancient legacy in traditional medicine/ethnopharmacology and are still frequently employed due to a diverse range of natural chemical sources. Different classes of bioactive molecules have been extracted and characterized, and in vitro and in vivo studies of various biochemical processes have been conducted(Rajesh et al., 2019). Similarly, this mangrove plant *B. gymnorhiza* has been recognized for so many years as one of the most important bioresources among the world's most profitable and ecologically complex environments since it plays an important role in forest conservation and protection, as well as future emergency or famine food in coastal regions. Ethnopharmacologically, it has been used to treat a variety of ailments(Musara et al., 2020). The plant parts treated with different extracts showed that it contains various phytochemical compounds. These phytochemicals protect human bodies against some pathogenic organisms and for this reason, they are the main target for drug prospecting programs. They are recognized to offer a variety of beneficial features for cells, including preventive, therapeutic, nutritional, and immune-modulatory effects(Rajesh et al., 2019). These phyto substances also demonstrated that various portions of the *B. gymnorhiza* plant extract contain chemical elements of pharmacological value, like the plant, has antidiabetic, antibacterial, antihemolytic, analgesic, antihyperlipidemic, hepatoprotective, and anticancer properties .which could play a vital role in pharmaceutical products development .

## Chapter 6-Conclusion and Future prospects

It has been found that there are many assays performed on the pharmacological activities of this plant which showed very positive results and some couldn't able to show because of shortages of advanced technology. Even, almost all in-vivo assays were performed on animals but there is no evidence found for any trial in humans. For this reason, more human trials by using some advanced scientific technology and artificial protocols are necessary as that can give more accuracy. Moreover, a stronger scientific explanation of those substances' processes, their molecular mechanisms, and therefore any drug interactions should be explored and further research is needed to supplement our current findings so that we can project the plant as a leading source of innovative medications. In recent years, herbal medications used around the world were found as a result of leads from traditional medicine. Even developed countries have recently begun to employ medicinal systems that include the use of herbal medications and cures. Plant-derived goods have undoubtedly grown in popularity around the world. Demand is expected to rise in the next years, owing to an increase in sales of herbal supplements and cures. Plant-derived drugs are used as traditional medicine over a long period of time but people don't retain any documents and information. Mostly passed down from generation to generation verbally. The World Health Organization (WHO) has shown a keen interest in recording tribals' use of medicinal plants from around the world. Many developing countries have stepped up their efforts to collect ethnomedical information on medicinal plants. People will be better informed about effective pharmacological therapy and improved health status once these local ethnomedical concoctions have been professionally tested and communicated effectively(Verma & Singh, 2008). As a result, the primary goal of this review is to make people acknowledge the pharmacological value of this plant. I am quite enthusiastic about a favorable result in future human testing because the assays (which were performed in a non-human host) looked very encouraging.Additionally, considering the number of phytonutrients discovered thus far, nature must have plenty more in the future. So many of these phytochemicals should be identified as synthesis methods improves and more advanced extraction and analysis techniques are developed(Kurmukov, 2013). Plants will always be a free community compound library with a large number of template molecules. It is, however, our duty to explore them in order to determine their undiscovered inherent healing qualities.

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